DESIRABLE FACTORS IN SURGICAL SUTURES

with special reference to

the absorbability of Surgical Catgut.

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Submitted to the

University of Edinburgh

as a Thesis

for the degree of Doctor of Philosophy

by

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March 1946.

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INTRODUCTION AND PURPOSE OF THE INVESTIGATION.

Lord Lister's work with surgical catgut, whereby he established the fact that it was absorbed and replaced by fibrous tissue, soon led to the observation that in certain tissues and conditions absorption took place comparatively rapidly and the need for "hardening" catgut in order to delay absorption became apparent.

Lister was probably the first to use a solution of chromic oxide and although he did so empirically with consequent uncontrolled variation in the degree of hardness of different batches of catgut, he did observe delayed absorption.[2, 9.]

From Lister's time until less than twenty years ago many different methods of sterilising and hardening surgical catgut were in use.[2] Heat sterilisation was not much used because experience then showed that an exposure to heat sufficient to give sterility usually reduced the tensile strength of the gut too far. In addition to processes involving the use of sporicidal aqueous solutions of iodine, inhibition of growth by means of essential oils, mercury salts etc., was commonly used; all such processes probably affected the rate of absorption of the catgut.

With /

With the application of the Therapeutic Substances Act Regulations to surgical catgut there was a tendency for production to be concentrated in the hands of a few manufacturers who had to obtain licences whereby their sterilisation processes were approved but there was no control over treatments intended to affect the rate of absorption; nor were tests prescribed to determine unintentional alterations in absorption rate due to sterilising procedures.

In recent years methods of heat sterilisation of catgut have been greatly improved. In the U.S.A. it is the most popular method, frequently being combined with the use of mercury and chromium compounds. In Britain, heat sterilisation is about as commonly used as chemical methods. In Europe, iodine sterilisation is the more generally employed though a combined bleaching and sterilising process involving the use of sulphur dioxide has been used in France.

Most manufacturers supply catgut of more than one absorption rate, some giving a definite indication of the absorption period e.g. "plain", "20-day", "30-day", others giving a general indication such as "unhardened", "mild chromic", "medium hardened" and so on. These absorption rates refer to normal muscle, e.g. lumbodorsal, it being understood that in more serous conditions /

conditions such as the intestines the catgut would be absorbed in one-third to one-quarter of the time.

There is reason to believe that methods of "hardening" catgut in order to alter its natural rate of absorption in the tissues are somewhat empirical, being based upon insufficient evidence regarding the fate of the sutures in living tissue. Further, it appears certain that methods of sterilisation used, whilst possibly excellent in themselves, cause unintentional alterations to the absorption rate of the sterile catgut.

It is also clear that amongst the well-known brands of surgical catgut on the market there are distinct types; for instance, the heavily chromicised heat-sterilised type; the lightly or unchromicised types; the chemically sterilised types, etc.

It seemed improbable that there could be uniformity among the absorption rates of such distinct catguts.

The uncertainty of this factor is reflected in the vagueness with which degrees of hardening are described in the United States Pharmacopoeia XII and in the Sixth Supplement (1944) to the British Pharmaceutical Codex, 1934.

Various workers, particularly in the U.S.A. have investigated /

investigated catgut absorption, commenting upon the varying rates of different makes and types.

Howes[1], in experiments on dogs, found that catgut in a clean wound resisted absorption for the required time according to the duration stated on the label of the material he used but in infected wounds the catgut, "plain", or "20-day", any gauge, lost strength with great rapidity. He did not report on the methods of sterilisation or of hardening which had been used for his material.

Jenkins[7] in a clinical study of catgut in relation to abdominal wound disruption noted a marked variation in resistance to absorption of different makes of "20-day" catgut but he did not investigate the reasons for this variation. He also suggested that the best and safest catgut would be that which could resist absorption in most of the operative conditions likely to be met with for at least 15 to 20 days, and that the use of the finest possible gauges would obviate foreign-body irritation with expulsion of knots if such catgut should last much longer than 20 days in clean wounds.

Wolff and Priestley[10] also found that absorption periods on catgut labels were fallacious and that certain brands of chromic catgut consistently lasted longer than others.

Jenkins /

Jenkins and others[17] conducted experiments in which they observed the absorption of catgut in the muscles of dogs and endeavoured to co-relate the results with tests on the rate of digestion of catgut in pepsin solution. Although some aspects of their technique may be open to criticism owing to the occurrence of undesirable side effects, much information was collected but, here again, no investigation was reported on the reasons why different catguts had differing or anomalous absorption periods - as for instance, what methods were used in making and sterilising, or the chemical constitution of the catgut.

PURPOSE OF THE PRESENT WORK.

1. To reproduce, by controlled manufacturing processes, the types of catgut found on the market and to compare them with well-known brands.

2. To find a practical and reliable method for determining the absorption rate of catgut in living animal tissue.

3. To devise an in vitro digestion test for catgut which might be comparable with the results obtained by tests in living tissue.

4. To investigate the chemical constitution of different /

different types of catgut and to find what, if any, explanation this may give for the occurrence of those types.

5. To note those characteristics of suture materials most likely to promote efficient wound repair.

Types of surgical catgut.

It has been observed[9] that while the need is admitted for chromicised catgut having a longer resistance to absorption than the unhardened material, practice varies considerably.

Before the outbreak of war in 1939 much of the catgut used in Europe was of German manufacture, mostly iodine-sterilised and seldom carrying any reference to absorption period. Chromic German catgut was hardly known and the labelling of the normal product corresponded to what we called "plain" catgut.

In Britain there were available unchromicised catguts and chromic varieties though these latter mostly contained a comparatively small proportion of chromium (0·05 per cent to 0·20 per cent calculated as Cr_2O_3), some heat-sterilised, some iodine-sterilised.

In the U.S.A. a large proportion of the catgut used was /

was heat-sterilised and highly chromicised (1·0 per cent to 1·5 per cent Cr_2O_3).

From the foregoing it would seem that European surgeons should frequently have experienced breakdown of wounds through premature absorption of stitches; American surgeons should have had trouble through prolonged resistance of the catgut to absorption, and the observations of British surgeons should have been intermediate.

The fact that such extreme results were not reported indicates that incidental factors were concerned which at least prevented premature absorption of the German product.

The question arises - What is "plain" catgut?

The B.P.C. 1934, Sixth Supplement 1944, says that it is catgut "which has not been processed so as to reduce the rate of absorption by the body tissue" and "is generally absorbed by normal muscle in from about five to ten days".

The U.S.P. XII 1942 refers to "plain gut which has not been treated in any manner which will alter its normal rate of digestibility", without indicating what that normal rate should be.

Experimental /

Experimental work to be described later shows that some types of catgut labelled "plain" are at least as resistant to absorption as others labelled "20-day" and Jenkins'[17] suggestion of the need for a standard plain catgut is endorsed.

Preparation of a standard plain catgut.

It is customary in catgut manufacture for various treatments to be given during the cleaning, splitting, scraping and twisting operations in order to facilitate removal of mesenteric tissue and mucous epithelium and to ensure ennearment of the component ribbons in the finished strands.

The chemicals used may include sodium carbonate, aluminium compounds, peroxides, etc. In addition, some makers introduce mercury salts or other bacteriostats. Most of these substances could affect the absorption period of the catgut strings.

In order to avoid these affects the standard plain catgut was made by using sheep intestines free from preservative of any kind and no chemicals were used up to the stage of splitting into ribbons.

As complete removal of unwanted layers of the intestinal coat is impracticable by mechanical means alone /

alone, a weak solution of sodium hydroxide (pH 9·0 to pH 10·0) was used at the stages of splitting and scraping. All traces of free alkali were removed by washing in water before the strings were twisted and dried.

The unsterile catgut thus produced was of good tensile strength but could not be so used for animal implants and it was therefore sterilised (after drying) by exposure in plugged tubes to toluol vapour under pressure at 150°C for five hours. After again drying to remove any condensed toluol the tubes were filled with 96% sterile alcohol and sealed. The catgut thus produced was sterile and still of excellent tensile strength.

This method of preparation and sterilisation was considered to be the least likely to have affected the absorption rate of the catgut and the product was accepted as Standard Plain catgut.

A Standard Plain catgut containing biniodide of mercury was also made by immersing the raw strings made as above in an aqueous solution of mercuric potassium iodide and then sterilising as described.

Other types were made to match those found in commerce including:-

A /

A heat-sterilised catgut containing a low proportion (0·1 per cent Cr_2O_3) of chromium introduced in the acidic state.

A heat-sterilised catgut containing a higher proportion (1·0 per cent Cr_2O_3) of chromium introduced in the basic state.

Catgut sterilised with aqueous iodine, the excess being decolorised by sodium thiosulphate solution and the products of "bleaching" removed by washing in water; referred to as iodine-sterilised plain (i).

Catgut sterilised with aqueous iodine, the excess being decolorised by sodium carbonate solution and the products of "bleaching" removed by washing in water; referred to as iodine-sterilised plain (ii).

A similarly sterilised catgut having a low proportion (0·05 per cent Cr_2O_3) of chromium introduced in the acidic state; referred to as iodine-sterilised hardened.

Various other combinations were possible, e.g. heat-sterilised chromic catgut containing biniodide of mercury, but these were not considered necessary for the present purpose.

A /

A complete list of samples used for the investigation is given below. It should be noted that catgut labelled "plain" is referred to as such; catgut labelled "chromic", "hard", "20-day", etc. is all referred to as "hardened".

1.	Standard Plain	Size	2/0	As already described.
2.	" "	"	2	" "
3.	Standard Plain with biniodide of mercury	"	2/0	" "
4.	Heat-sterilised (0·1 per cent Cr_2O_3)	"	2/0	" "
5.	Heat-sterilised (1·0 per cent Cr_2O_3)	"	2/0	" "
6.	Heat-sterilised (1·0 per cent Cr_2O_3)	"	2	" "
7.	Iodine-sterilised plain (i)	"	2/0	" "
8.	Iodine-sterilised plain (ii)	"	2/0	" "
9.	Iodine-sterilised hardened	"	2/0	" "
10.	Brand A plain	"	2/0	Commercial product.
10a.	" A hardened	"	2/0	" "
11.	Brand B plain	"	2/0	" "
11a.	" B hardened (i)	"	2/0	" "
11b.	" B hardened (ii)	"	2/0	" "
12.	Brand C plain	"	2/0	" "
12a.	" C hardened	"	2/0	" "

13 /

13.	Brand D plain	Size 2/0	Commercial product.
13a.	" D hardened	" 2/0	" "
14.	Brand E plain	" 2/0	" "
14a.	" E hardened	" 2/0	" "

CHOICE OF GAUGE FOR THE INVESTIGATION.

The work has been conducted primarily with catgut of gauge 2/0 (B.P.C. and U.S.P. standards) because it is known that thicker gauges may introduce complicating factors such as excessive "reaction" and because the use of thicker catgut is believed to have no advantage.

A tendency to use thick catgut at operation is due to an unfounded fear that fine stitches may be insufficiently strong to hold the wound edges in apposition. Great force is not normally necessary to keep a wound closed and even if considerable strain is expected, e.g. retching or coughing after laparotomy, it is more likely that the sutures would cut out of the tissues than that the stitches themselves would break.

The shearing strain of tissues, which is analogous to their resistance to the cutting out of stitches, is not so high as appears to be generally believed, varying from less than 1 lb. in soft tissue, e.g. bowel, to no more /

more than $2\frac{1}{4}$ lb. in rectus muscle sheath. The minimum standard breaking strain for No. 2/0 catgut (B.P.C.) even when knotted is $2\frac{1}{2}$ lb.

Howes and Harvey[3], referring to the use of interrupted catgut stitches for repair of ventral herniae, concluded that considerable tension constantly maintained would undoubtedly lead to the cutting out of stitches. From experiments on the resistance of tissues to tearing stresses they recommended catgut No. 0 for fascia and No. 3/0 for muscle and peritoneum.

In an article entitled "How to use catgut" Howes[16] advised gauge 0 for fascia, 3/0 for muscle, 4/0 for subcutaneous tissue and 5/0 for mucous membrane.

A greater use of gauge 5/0 was recommended also by Bower, Burns and Mengle[13].

The possibility of loss of strength by suture materials solely through the wetting action of the tissues was investigated by Howes[14] but his experiments confirmed his belief that catgut thicker than No. 0 is never necessary.

Thick strands are contra-indicated also because of a greater tendency to cause a reaction which is usually manifested by an accumulation of sterile detritus, though this is more marked the more "plain" the catgut.

This /

This reaction accords with the first phase of absorption (invasion of the catgut by large numbers of polymorphonuclear leucocytes) noted by Jenkins[17]. In more resistant samples this first phase is little evidenced and is replaced by the second, slower, mechanism whereby the stitches are surrounded and invaded by macrophages with little or no detritus.

Suspected infection in a wound need not be a reason for using thick catgut; besides the addition of "thick catgut reaction" to the bacterial disturbance it is by no means certain that a moderate infection speeds up the absorption of catgut excessively.

Although Howes[1] found that catgut in infected wounds lost strength rapidly, Wolff and Priestley[10] stated that suppurating wounds did not cause early absorption and Jenkins[7], in a survey of a large number of abdominal wound disruptions, found that the cases in which infection was present disrupted considerably later than the clean cases.

ABSORPTION OF CATGUT IN LIVING TISSUE.

Whatever other means of controlling the absorption rate of surgical catgut may be devised, the criterion is the result of its use in living tissue.

Reports /

Reports on catgut absorption in the human body are comparatively scarce; for every instance of some interesting effect there must be thousands of cases in which no further thought needed to be given to the catgut once the wound was sutured.

Jenkins[7] used the "Seton method" in clean laparotomies. Interrupted stitches of the catgut under test were put into the abdominal muscle, one end of each stitch being cut close to the knot and the other end led to the surface through a needle puncture in the skin to the side of the wound incision; the free end of the catgut was gently pulled from time to time until it came away. Results for four different brands of chromic catgut varied from six to twenty days. Apparently no mechanical check was made on the force of the "gentle pulls" and no analytical data are given regarding the types of chromic catgut.

Wolff and Priestley[10] used a modification of Jenkins' method. One or more interrupted catgut sutures were placed through the anterior fascia of the rectus muscle and, passing below the catgut knot, was a loop of non-absorbable material which was permitted to project from the skin. "Gentle traction" was applied every day or two until the loop of non-absorbable material came away. From a series of 358 stitches tested in 164 patients and observing the influence of infection /

infection, age, cachexia, etc., a number of interesting conclusions were drawn including:-

Fine gauges lasted as long as thick ones.

Single strands lasted as long as double ones.

Suppuration and drainage (? sterile or unsterile) did not accelerate catgut absorption.

Absorption periods stated on labels were fallacious.

Because of the natural unwillingness of patients to be the subject of wound experiments and the difficulty of applying mechanical control of tension tests to human beings it is more practicable to base a standard living tissue technique on mammals with a metabolism closely similar to that of human beings. As a regular supply of dogs of similar size and age was not available the animals chosen for the present series were male rabbits from six to twelve months old.

OPERATIVE PROCEDURE.

The rabbits were deprived of food for 24 hours before operation, drinking water being freely available.

Anaesthesia was induced by Nembutal, intravenously, followed by a light application of open ether as required.

Operation /

Operation sites were prepared by shaving and liberally painting the skin with solution of iodine which was allowed to dry for two or three minutes before incising.

Full aseptic precautions were taken throughout in order that the conditions for each operation should be identical with those obtaining in normal surgical practice. No antiseptics or bactericides were introduced into the wounds as many of these could affect the absorption rate of the catgut stitches.

All suturing, except for the catgut under test, was done with non-capillary braided silk. After closure the wound site was painted with iodine solution and covered with a layer of sterile gauze impregnated with 1 : 1000 sterile acriflavine solution and held in place by adhesive strapping. In order to prevent interference by the animal with the dressing a linen jacket was used; this was designed to permit free movement of the limbs and was removed 3 or 4 days after operation - that is as soon as immediate post-operative irritation had subsided, after which the rabbits seldom attempted to remove the adhesive strapping.

No animal was used for more than one set of implants in order to eliminate possible sensitivity effects. It may be noted, however, that Kraissl[6] found that /

that very few normal patients showed sensitivity to catgut and he thought those who did would be likely to have a history of allergy; Hopps[20] reported that large quantities of catgut were required to produce sensitivity in animals.

Method of implanting catgut in animals.

It is desirable that the technique used should closely follow in essential details the manner in which catgut is used in actual wound repair.

Howes[1] threaded lengths of catgut beneath the serosa of a dog's stomach, later removing them for machine tests of residual tensile strength. Jenkins and others[17] in their earlier experiments inserted six inch lengths of catgut longitudinally into the abdominal muscles of dogs, removing the strands later for breaking strain tests.

The serious objection to this method as opposed to making actual stitches is that, the ends being free, the catgut untwists under the influence of moisture from the tissues; this opening of the strand soon multiplies many times the surface area upon which body enzymes can act with a proportionate speeding up in the rate of digestion.

EXPERIMENT /

EXPERIMENT A - 1. Standard Plain No. 2/0 catgut was implanted intramuscularly by threading through the abdominal muscle and intermuscularly by laying the strand in a longitudinal incision and closing the muscle over it with silk. About 1½ in. of the catgut strands were in the muscle and the free ends projected from the surface of the skin.

A strain of 450 grammes was applied daily to the free ends of each strand; the intermuscular implant breaking on the 5th day and the intramuscular on the 6th.

The different results obtained by the standard stitch technique developed later confirm the false premise of the longitudinal implants.

Methods of observing rate of absorption of catgut.

It is acknowledged that surgical catgut is gradually digested by body enzymes, its tensile strength slowly diminishing until fragmentation occurs and ultimately the whole stitch ceases to exist.

In experimental work it is necessary to decide at what stage of absorption the catgut shall be deemed to have lost its usefulness.

Howes[1] found that the rate of loss of holding

power /

power of catgut in the tissues was not properly indicated by its appearance and that mechanical testing was desirable.

Jenkins and others[17] in their longitudinal implant experiments found that the loss of tensile strength of catgut in the tissues was proportional to the time. When they implanted by means of interrupted stitches they used an arbitrary scale based on appearance e.g. stitch intact; slight fraying; continuity broken; knot only remaining, etc. This method is not considered satisfactory because of two catgut stitches both looking partly digested, one may have a holding power several times that of the other. It was decided that a mechanical test was necessary.

Based upon the shearing strains of tissues (p. 12) and having regard to the fact that, as catgut stitches lose strength by absorption the force necessary to hold the wound edges in apposition is lessening through the formation of granulation tissue, a breaking strain of 450 grammes was selected as the holding power below which catgut would have lost its usefulness for normal suturing purposes in muscle.

Trial implant techniques.

It /

It was decided to try to use on rabbits the "Seton method" used by Jenkins[7] in human laparotomy wounds (p. 15). The apparent advantage of this method was that it allowed tests to be made at frequent intervals with the minimum of shock to the animal.

EXPERIMENTS A - 2 to A - 13 inclusive. Various factors which resulted in the "Seton method" being later discarded detract from the value of this group of experiments and make it unnecessary to describe them in detail. The experience gained is summarised as follows.

Interrupted stitches of the catgut under test were put into the abdominal muscle. Through each stitch was passed a piece of non-capillary silk which was brought out through a hole to the side of the skin incision. Daily, or as required, the hook of an accurate spring balance was inserted into a loop in the silk and a strain of 450 grammes applied.

Some of the operations were performed before the linen jacket (p. 17) had been brought into use and the experiments were spoiled through the animals removing the protective plaster and biting through the projecting silk loops.

Two experiments were abandoned because the wounds became infected (Staphylococcus albus) through contamination /

ation from the skin surface being carried to the subcutaneous layers as the silk loops moved in and out of the holes in the skin.

TABLE 1.

Summary of tests on rabbits by "Seton method" in Experiments A - 2 to A - 13.

Catgut	5th to 10th day	11th to 15th day	16th to 20th day	21st to 30th day	Over 30 days after operation.
Apparently absorbed					
Standard Plain 2/0	3	4	2	1	-
Iodine-sterilised plain (ii) 2/0 and Iodine-sterilised hardened 2/0	1	-	-	1	1
Heat-sterilised 2/0 (1·0% Cr_2O_3)	-	3	1	3	-
Cut out, partially digested					
Standard Plain 2/0	1	1	4	1	-
Iodine-sterilised plain (ii) 2/0 and Iodine-sterilised hardened 2/0	2	1	-	2	2
Heat-sterilised 2/0 (1·0% Cr_2O_3)	-	-	-	1	-
Cut out, no apparent absorption					
Standard Plain 2/0	-	1	-	-	-
Iodine-sterilised plain (ii) 2/0 and Iodine-sterilised hardened 2/0	2	-	-	-	-
Heat-sterilised 2/0 (1·0% Cr_2O_3)	1	-	-	-	-

From Table 1, above, it will be seen that frequent testing, even to 450 grammes, caused nearly fifty per cent of the stitches to cut out.

The method is not reliable as an animal implant test for the rate of absorption of surgical catgut. It was clear that frequent testing must be avoided and that the use of the silk loops was undesirable owing to the risk of infection being carried from the skin surface to the site of the stitches.

EXPERIMENTS A - 14 and 15 were conducted to ascertain the suitability of the lumbar muscles for catgut implants. It was found that muscle incisions could be made and closed with the test sutures and the skin and sub-cutaneous tissues repaired with non-capillary silk. The animals recovered quickly and there was no interference with the linen jackets or dressings.

STANDARD TECHNIQUE FOR ANIMAL IMPLANTS.

The technique adopted as a standard method was essentially the implanting of interrupted test stitches in incised lumbar muscle. The stitches were tested twice at selected periods after implanting.

The first test was made at re-operation using full aseptic /

aseptic precautions. Care was taken to see that the surface of each stitch was free from adherent tissue, the hook of a spring balance was inserted near the knot and a strain of 450 grammes applied for about 15 seconds. The wound was re-closed and the second test made at post mortem examination. On this occasion, if a stitch did not break at 450 grammes, tension was slowly increased to 1350 grammes.

It was considered undesirable to re-operate on any animal more than once, partly on ethical grounds and partly because too frequent testing had itself been shewn to lead to inaccurate results.

When implanting, an incision 2 in. to $2\frac{1}{2}$ in. long and $\frac{1}{8}$ in. to $\frac{1}{4}$ in. deep was made in the lumbar muscle on each side of the spine. These incisions were then closed with interrupted stitches of the test catgut (usually 5 each side) the tension applied being just sufficient to close the muscle wound, including the muscle sheath; the distance between the points of emergency of the stitch was about $\frac{3}{8}$ in. giving room for the insertion of the hook of the spring balance when testing.

At least two varieties of catgut were tested in each animal and each variety was tested in more than one animal the results thus cross-checking to detect any exceptional /

exceptional idiosyncrasy.

EXPERIMENTS A - 16 to 21, 23, 25 to 27, 30, 33 to 48, 50 - 64, 72. These were all animal implants conducted according to the standard technique described above; the results are summarised in Table 2.

TABLE 2.

Summary of animal implant experiments.

Explanation of signs:-

< 450 = stitches broke below a strain of 450 grammes.

> 450 = stitches withstood a strain of 450 grammes (or 1350, etc.).

x 900/1125 = stitches broke between 900 and 1125 grammes (or 1125/1350, etc.).

Note:-

450 grammes = 1 lb. approx. and chosen for reasons given in the text.

675 grammes = 1½ lb. approx.

900 " = 2 lb. " .

1125 " = 2½ lb. " .

1350 " = 3 lb. " .

TABLE 2 (Continued).

CATGUT SAMPLE	EXPT.	DAYS AFTER IMPLANTING 14th	21st	28th	35th	42nd	49th	56th
Standard Plain No.2/0	A-16	3 < 450 2 > 450	2 < 450					
" "	A-17	5 > 450	2 < 450 2 x 450/675 1 x 675/1125					
" "	A-20	5 > 450	1 x 450/675 4 x 900/1125					
" "	A-21	3 < 450 2 > 450	2 < 450					
" "	A-33	1 < 450 4 > 450	3 < 450 1 x 675/900					
" "	A-34		2 < 450 3 > 450	3 < 450				
" "	A-39	5 > 450	4 < 450 1 x 450/675					
Standard Plain No.2	A-58			3 < 450 2 > 450	1 < 450 1 x 675/900			
" /								

TABLE 2 (Continued).

CATGUT SAMPLE	EXPT.	DAYS AFTER IMPLANTING 14th	21st	28th	35th	42nd	49th	56th
Standard Plain No. 2	A-61	5 > 450	5 x 900/1125					
" "	A-64	5 > 450		4 < 450 1 x 675/900				
Standard Plain with HgI_2 No.2/0	A-61	5 > 450	1 x 675/900 4 x1125/1350					
" "	A-62		5 > 450	2 x 675/900 2 x 900/1125 1 x1125/1350				
Heat-sterilised (0·1%Cr_2O_3) No2/0	A-60	5 > 450	3 < 450 2 x 675/900					
" "	A-62		5 > 450	3 x 450/675 2 x 675/900				
Heat-sterilised (1·0%Cr_2O_3) No2/0	A-16	5 > 450	2 < 450 2 x 450/675 1 x 675/1125					
" "	A-18		1 < 450 4 > 450	4 < 450				
" /								

TABLE 2 (Continued).

CATGUT SAMPLE	EXPT.	DAYS AFTER IMPLANTING 14th	21st	28th	35th	42nd	49th	56th
Heat-sterilised ($1.0\%Cr_2O_3$) No 2/0	A-23		5 > 450	2 < 450 3 x 450/675				
" "	A-25		5 > 450	4 < 450 1 x 450/675				
" "	A-30			4 > 450 1 < 450		4 < 450		
" "	A-35	5 > 450	1 < 450 1 x 675/900 3 > 1350					
" "	A-36		5 > 450	2 x 450/675 2 x 675/900 1 x 900/1125				
" "	A-41			5 < 450				
" "	A-47			5 > 450	5 < 450			
" "	A-51		1 < 450 4 > 450	2 < 450 2 x 450/675				

" /

TABLE 2 (Continued).

CATGUT SAMPLE	EXPT.	DAYS AFTER IMPLANTING 14th	21st	28th	35th	42nd	49th	56th
Heat-sterilised ($1{\cdot}0\%Cr_2O_3$) No2/0	A-52		2 < 450 3 > 450	3 < 450				
" "	A-53			5 < 450				
" "	A-59			2 < 450 3 > 450	3 < 450			
Heat-sterilised ($1{\cdot}0\%Cr_2O_3$) No.2	A-59			5 > 450	5 x1125/1350			
" "	A-60	5 > 450	2 x1125/1350 3 >1350					
Iodine-sterilised plain (i) No.2/0	A-17	5 > 450	5 >1350					
" "	A-18		1 < 450 4 > 450	4 >1350				
" "	A-26			5 > 450	1 x 450/675 1 x 675/900 3 x 1125/1350			
" /								

TABLE 2 (Continued).

CATGUT SAMPLE	EXPT.	DAYS AFTER IMPLANTING 14th	21st	28th	35th	42nd	49th	56th
Iodine-sterilised plain (i) No.2/0	A-27				3 < 450 2 > 450		1 x 450/675 1 x 675/900	
" "	A-43					3 < 450 2 > 450		2 < 450
" "	A-44				2 < 450 3 > 450		3 < 450	
Iodine-sterilised plain (ii) No.2/0	A-19		5 > 450	5 > 1350				
" "	A-26			5 > 450	1 < 450 2 x 675/900 2 x 900/1125			
" "	A-27				1 < 450 4 > 450		2 x 450/675 2 x 675/900	
" "	A-43					5 > 450		5 < 450
" "	A-45				2 < 450 3 > 450		3 < 450	
" /								

TABLE 2 (Continued).

CATGUT SAMPLE	EXPT.	DAYS AFTER IMPLANTING 14th	21st	28th	35th	42nd	49th	56th
Iodine-sterilised hardened No.2/0	A-19		5 > 450	5 >1350				
" "	A-50					5 > 450		1 < 450 3 x 450/675 1 x1125/1350
" "	A-56			5 > 450		5 >1350		
" "	A-64	5 > 450		5 >1350				
Brand A plain No.2/0	A-33	1 < 450 4 > 450	1 < 450 3 x 675/900					
" "	A-34		4 < 450 1 > 450	1 < 450				
Brand A hardened No.2/0	A-35	5 > 450	3 < 450 2 x 450/675					
" "	A-36		2 < 450 3 > 450	2 < 450 1 x 450/675				

Brand /

TABLE 2 (Continued).

CATGUT SAMPLE	EXPT.	DAYS AFTER IMPLANTING 14th	21st	28th	35th	42nd	49th	56th
Brand B plain No.2/0	A-54				4 < 450 1 > 450		1 < 450	
" "	A-57		2 < 450 3 > 450		3 < 450			
" "	A-63	2 < 450 3 > 450		1 < 450 2 x 900/1125				
Brand B hardened (i) No.2/0	A-20	5 > 450	5 > 1350					
" "	A-40		5 > 450	5 > 1350				
" "	A-44				1 < 450 4 > 450		3 < 450 1 x 675/900	
" "	A-46			2 < 450 3 > 450	3 > 1350			
Brand B hardened (ii) No.2/0	A-23		5 > 450	5 > 1350				
" /								

TABLE 2 (Continued).

CATGUT SAMPLE	EXPT.	DAYS AFTER IMPLANTING 14th	21st	28th	35th	42nd	49th	56th
Brand B harden-ed (ii) No.2/0	A-30			5 > 450		3 < 450 2 x 450/675		
" "	A-45				5 < 450			
" "	A-47			1 < 450 4 > 450	2 < 450 2 x1125/1350			
Brand C plain No. 2/0	A-37	5 >450	1 x 450/675 4 x 675/900					
" "	A-38		5 > 450	3 < 450 1 x 450/675 1 x 675/900				
" "	A-58			5 > 450	3 < 450 2 x 900/1125			
Brand C harden-ed No. 2/0	A-39	5 >450	1 x 450/675 4 >1350					
" "	A-40		5 > 450	2 x 675/900 3 x1125/1350				
" /								

TABLE 2 (Continued).

CATGUT SAMPLE	EXPT.	DAYS AFTER IMPLANTING 14th	21st	28th	35th	42nd	49th	56th
Brand C hardened No. 2/0	A-55				5 >450	5 >1350		
Brand D plain No. 2/0	A-51		5 >450	5>1350				
" "	A-55				5 >450	5 >1350		
" "	A-56			5 >450		1 x1125/1350 4 >1350		
Brand D hardened No. 2/0	A-52		5 > 450	5>1350				
" "	A-53			5 >450		5 >1350		
" "	A-50					5 > 450		1 x 900/1125 2 x1125/1350 1 >1350
" "	A-54				5 >450		5 >1350	
Brand E plain No. 2/0	A-21	5 > 450	5>1350					
" /								

TABLE 2 (Continued).

CATGUT SAMPLE	EXPT.	DAYS AFTER IMPLANTING 14th	21st	28th	35th	42nd	49th	56th
Brand E plain No. 2/0	A-38		2 < 450 3 > 450	3 < 450				
" "	A-48				5 < 450			
" "	A-41			5 < 450				
Brand E hardened No. 2/0	A-25		4 < 450 1 > 450	1 < 450,				
" "	A-37	5 > 450	2 x 450/675 2 x 900/1125 1 >1350					
" "	A-46			2 < 450 3 > 450	3 < 450			

DEDUCTIONS FROM ANIMAL IMPLANT EXPERIMENTS.

In order to condense the experimental data, Table 3 has been drawn up to show the "peaks" and "spread" of absorption periods found for different catguts.

Following this, Table 4 shows a further simplification in which the various samples have been divided into three absorption-period groups, namely -

Group I Majority of stitches reduced to a holding power less than 450 grammes within 28 days.

Group II Majority of stitches reduced to a holding power less than 450 grammes between 21 and 35 days.

Group III Majority of stitches NOT reduced to a holding power less than 450 grammes until more than 35 days after implanting.

It would appear that three absorption-period groups are the maximum that should be attempted; indeed, it is probable that the ordinary requirements of the surgeon would be amply met by only two groups.

A discussion concerning the anomalous occurrences of "plain" and "hardened" catgut in absorption Groups I, II and III will be found later, p. 77, in connection with the chemical analyses.

Careful /

Careful observations have been made during the course of these experiments in order to detect incidental factors which might vitiate the reliability of the results. Within the limits of biological variation and keeping conditions as close as possible to those obtaining when catgut is used in human tissues, the technique adopted appears to give reliable results.

TABLE 3.

CATGUT ABSORPTION RATES IN UNCONTAMINATED RABBIT MUSCLE BASED ON EXPERIMENTS A - 16, ONWARDS.

CATGUT SAMPLE	7 to 14 days	14 to 21 days	21 to 28 days	28 to 35 days	35 to 49 days	49 to 63 days	over 63 days
Standard Plain No.2/0	20%	43%	37%	-	-	-	-
Standard Plain No.2	-	-	70%	20%	10%	-	-
Standard Plain with HgI_2 No.2/0	-	-	10%	80%	10%	-	-
Heat-sterilised (0·1%Cr_2O_3) No.2/0	-	30%	20%	50%	-	-	-
Heat-sterilised (1·0%Cr_2O_3) No.2/0	-	11%	52%	31%	6%	-	-
Heat-sterilised (1·0%Cr_2O_3) No.2	-	-	-	20%	-	80%	-
Iodine-sterilised plain (i) No. 2/0	-	5%	-	29%	33%	33%	-
Iodine-sterilised Plain (ii) No. 2/0	-	-	-	20%	35%	45%	-

Iodine /

TABLE 3 (Continued).

CATGUT SAMPLE	7 to 14 days	14 to 21 days	21 to 28 days	28 to 35 days	35 to 49 days	49 to 63 days	over 63 days
Iodine-sterilised hardened No. 2/0	-	-	-	-	-	10%	90%
Brand A plain No.2/0	10%	50%	40%	-	-	-	-
Brand A hardened No. 2/0	-	50%	40%	10%	-	-	-
Brand B plain No.2/0	13%	13%	7%	60%	7%	-	-
Brand B hardened (i) No. 2/0	-	-	20%	10%	60%	10%	-
Brand B hardened (ii) No. 2/0	-	-	6%	47%	47%	-	-
Brand C plain No.2/0	-	-	53%	33%	14%	-	-
Brand C hardened No. 2/0	-	-	17%	33%	50%	-	-
Brand D plain No.2/0	-	-	-	-	-	20%	80%
Brand D hardened No. 2/0	-	-	-	-	-	-	100%
Brand E plain No.2/0	-	13%	54%	33%	-	-	-
Brand E hardened No. 2/0	-	27%	47%	20%	6%	-	-

Note: Where stitches at post-mortem examination broke below 1125 gm., count 1 period later.

Where stitches at post-mortem examination broke 1125/1350 gm., count as 2 periods later.

TABLE /

TABLE 4.

CATGUT ABSORPTION GROUPS BASED ON TABLE 3.

CATGUT SAMPLE	GROUP I	GROUP II	GROUP III
Standard Plain No. 2/0	+		
" " " 2	+		
Brand A plain No. 2/0	+		
" A hardened No. 2/0	+		
Brand E hardened No. 2/0	+		
Standard Plain with HgI_2 No. 2/0		+	
Heat-sterilised (0·1%Cr_2O_3) No. 2/0		+	
Heat-sterilised (1·0%Cr_2O_3) No. 2/0		+	
Brand B plain No. 2/0		+	
" B hardened (ii) No. 2/0		+	
Brand E plain No. 2/0		+	
Brand C plain No. 2/0		+	
Iodine-sterilised plain (i) No. 2/0			+
Iodine-sterilised Plain (ii) No. 2/0			+
Iodine-sterilised hardened No. 2/0			+
Heat-sterilised (1·0%Cr_2O_3) No. 2			+
Brand B hardened (i) No. 2/0			+
Brand C hardened No. 2/0			+
Brand D plain No. 2/0			+
" D hardened No. 2/0			+

CATGUT /

CATGUT REACTION.

The general observations of previous workers have been to the effect that plain catgut caused more reaction than hardened types and thick strands more than fine ones; this accords with the report of Jenkins and others[17] on the mechanism of absorption in the tissues.

The results of my own animal implant experiments agree with this in principle though, as most of the tests were made with size 2/0, there was very little reaction as evidenced by detritus. Where detritic reaction was marked, as in thick Standard Plain catgut (No. 2), the matter was tested bacteriologically and found in every instance to be sterile.

Reaction tended to occur more with catgut which came into absorption Group I. It is noteworthy that most of the resistant stitches in size 2/0 were clean and free from irritation throughout.

There has been a number of papers suggesting that various non-absorbable suture materials are all preferable to catgut[12, 15, 18, 19], mostly claiming their freedom from irritation to the tissues. As detritic reaction with catgut, when it does occur, usually appears within a few days of operation it was decided to implant some non-absorbable sutures and compare them with a type of catgut which had been noted for its non /

non-irritant qualities. Slight detritus is soon re-absorbed and it seemed probable that its reported absence with non-absorbable suture materials was due to the fact that experimental wounds had not been examined at an early stage.

EXPERIMENTS A - 68 to 70. Using the technique adopted for catgut implants, but without making tensile strength tests, various non-absorbable materials were compared with heat-sterilised (1·0 per cent Cr_2O_3) catgut No. 2/0 at re-operation after 7 days and at post-mortem examination after 14 days. The results are summarised in Table 5.

TABLE 5.

IMPLANTS OF NON-ABSORBABLE SUTURES IN RABBIT MUSCLE COMPARED WITH CATGUT.

MATERIAL	RABBIT	AFTER 7 DAYS	AFTER 14 DAYS
Heat-sterilised catgut (1·0%Cr_2O_3) No. 2/0	A-68) A-69) A-70)	clean) clean) clean)	clean) clean) clean)
Nylon No.1(N)	A-68	marked detritus)	cleaner
Nylon No. 8(N)	A-69	detritus	cleaner
Silkworm, ophthalmic	A-68	clean	clean
Silkworm, stout	A-69	detritus	no change
Cotton No. 4/0	A-68	clean	clean
Cotton No. 3/0	A-69	detritus	clean
Unproofed silk No. 0	A-70	clean	clean
Non-capillary silk No. 0	A-70	clean	clean
Linen thread No. 100	A-70	detritus	clean

In /

In each case where detritus occurred bacteriological tests gave a negative result.

ABSORPTION OF CATGUT IN PRESENCE OF GASTRIC JUICE.

As in vitro work on catgut using pepsin solutions has shown digestion to take place rapidly (see later), it follows that catgut used in gastrotomy would, if allowed to pass through to the lumen of the stomach, be absorbed within a very short period.

EXPERIMENTS A - 22, 24, 28. In these, an abdominal incision was made to the left of the mid-line to expose the stomach, sterile saline packs being used as necessary. Three interrupted stitches each of two samples of catgut were inserted through the gastric wall having partial contact with the stomach contents. The abdominalwall and skin were closed with non-capillary silk in the usual way.

The catguts tested in the three rabbits were Standard Plain No. 2/0, heat-sterilised (1·0 per cent Cr_2O_3) No. 2/0 and iodine-sterilised plain (i) No. 2/0. At re-operation after only four days digestion had taken place in every instance and the remains of the stitches were lying loose.

Although wounds of the stomach wall heal with great /

great rapidity the above experiments suggest that an absorbable suture may be contra-indicated where the stitches come into contact with the gastric juices.

CATGUT IN INFECTED WOUNDS.

Previous workers having disagreed (p. 14) over the influence of bacterial infection on the rate of catgut absorption, four experiments were performed using four basic types of catgut and the commercial brand which had shown the longest absorption period in the standard muscle implants.

EXPERIMENTS A - 65 to 67 and 72. The previously described technique for lumbar muscle implants was followed except that the muscle incisions were liberally infected with a 24-hour mixed culture of active but non-pathogenic strains of Staph. albus: (Staphylococcus albus, strains 105 and 180, University of Edinburgh Bacteriology Dept.). In Experiment 67 ordinary and non-capillary silk were also implanted.

Tensile strength tests were made in the usual way. Where an excessive amount of detritic matter was found at re-operation the wound was cleaned with dry sterile gauze; at both re-operation and post-mortem examination swabs were taken and cultured and heavy growths obtained in every instance.

The /

The infective reaction in each animal was severe and provided a good test of the effect of aerobic infection on catgut absorption. Each animal had gained control over the infection as shown by wound appearance between re-operation and post-mortem examination though the continued presence of viable Staph. albus was demonstrated.

A summary of the results obtained is shown in Table 6 and from this Tables 7 and 7a have been drawn up to show that although the infection led to earlier absorption of the catgut it did not do so to any great extent. Only one of the types of catgut tested was moved into an earlier absorption Group than that found for uncontaminated wounds.

TABLE 6.

EXPERIMENTS A - 65 to 67, 72. SUMMARY OF RESULTS.

Explanation of signs:-

< 450 = stitches broke below a strain of 450 grammes.

> 450 = stitches withstood a strain of 450 grammes (or 1350, etc.).

x 900/1125 = stitches broke between 900 and 1125 grammes (or 1125/1350, etc.).

Note:- 450 grammes = 1 lb. approx. and chosen for reasons given in the text.

675 grammes = 1½ lb. approx.

900 " = 2 lb. " .

1125 " = 2½ lb. " .

1350 " = 3 lb. " .

TABLE 6 (Continued).

SUTURE	EXPT.	DAYS AFTER IMPLANTING 7th	14th	21st	35th
Standard Plain No.2/0	A-65	3 > 450		3 < 450	
" "	A-66		1 < 450 2 > 450		No trace
Standard Plain with HgI_2 No.2/0	A-65	3 > 450		2 x 450/675 1 x 900/1125	
" "	A-66		3 > 450		3 < 450
" "	A-72	5 > 450	2 < 450 1 x 675/900 1 x 900/1125		
Heat-sterilised ($1\cdot0\%Cr_2O_3$) No2/0	A-65	3 > 450		2 < 450 1 x 450/675	
" "	A-67		2 < 450 1 > 450	1 < 450	
" "	A-72	5 > 450	1 < 450 2 x 675/900 2 x1125/1135		
Iodine /					

TABLE 6 (Continued).

SUTURE	EXPT.	DAYS AFTER IMPLANTING 7th	14th	21st	35th
Iodine-sterilised hardened No.2/0	A-65	3 > 450		3 > 1350	
" "	A-66		3 > 450		1 < 450 2 x 675/900
Brand D hardened No. 2/0	A-66		3 > 450		3 > 1350
" "	A-67		3 > 450	3 > 1350	
*Non-capillary silk No. 2	A-67		3 > 450	3 > 1350	
*Ordinary silk No. 2	A-67		3 > 450	3 > 1350	

* It is noteworthy that, whereas the ordinary silk was embedded in masses of exudate, the non-capillary silk was not apparently acting as a focus for the infecting organisms.

TABLE /

TABLE 7.

CATGUT ABSORPTION RATES IN INFECTED WOUNDS BASED ON EXPERIMENTS A - 65 to 67 and 72.

CATGUT SAMPLE	7 to 14 days	14 to 21 days	21 to 35 days	over 35 days
Standard Plain No. 2/0	17%	83%	-	-
Standard Plain with HgI_2 No. 2/0	18%	27%	55%	-
Heat-sterilised (1·0% Cr_2O_3) No. 2/0	27%	46%	27%	-
Iodine-sterilised hardened No. 2/0	-	-	17%	83%
Brand D hardened No. 2/0	-	-	-	100%

TABLE 7a.

EFFECT OF CONTAMINATION ON CATGUT ABSORPTION GROUPS.

CATGUT SAMPLE	GROUP IN TABLE 4	GROUP ACCORDING TO TABLE 7
Standard Plain No. 2/0	I	I
Standard Plain with HgI_2 No. 2/0	II	II
Heat-sterilised (1.0%Cr_2O_3) No. 2/0	II	I
Iodine-sterilised hardened No. 2/0	III	III
Brand D hardened No. 2/0	III	III

NOTE: Although heat-sterilised (1·0%Cr_2O_3) catgut was moved from Group II to Group I, Standard Plain with HgI_2 retained its position in Group II.

IN VITRO DIGESTION TESTS.

Purpose of the tests.

Various workers[5, 6, 17] have described attempts to devise in vitro digestion tests which would determine catgut absorption rates without resorting to implants in living animals.

Choice of enzyme.

The enzymes which can be used for these tests are restricted, trypsin and pepsin being the most suitable.

Of these, trypsin has the advantage of acting in alkaline solution and thus resembles the mechanism by which catgut is absorbed in living tissues. Unfortunately this enzyme has two serious disadvantages. One is that standardisation is impracticable and the commercial product varies from batch to batch; the other is that the alkaline conditions necessary predispose the solution to active bacterial growth.

This bacterial growth is highly undesirable because it produces uncontrollable factors which will almost certainly interfere with the tests; it might be removed by micro-filtration but the stringent conditions necessary to prevent re-infection during the test would be difficult to achieve. The addition of inhibitory substances /

substances has been suggested by Kraissl[6] but is not recommended because they may introduce a further unknown effect.

Pepsin, on the other hand, can be standardised fairly accurately and, requiring an acid solution, does not encourage bacterial growth. Its main disadvantage is that, being an acid enzyme, its digestive action on catgut may not be directly comparable with the alkaline absorptive action of the tissues. It was decided that pepsin would be the more suitable enzyme to use in the present experiments.

The material used throughout has been the commercial product known as "10000 test".

Enzyme solution.

Jenkins and others[17] used a 10 per cent aqueous solution of Pepsin U.S.P. XI ("3000/3500 test") containing 1 millilitre of concentrated hydrochloric acid. They do not appear to have controlled the pH accurately.

EXPERIMENT D - 1. This was undertaken to find the optimum conditions of pH and enzyme concentration for catgut digestion tests.

All factors other than pepsin concentration and pH were kept constant.

Standard /

Standard Plain catgut, No. 2/0, was used and single strands, each supporting a separate 35 gramme lead weight were exposed in individual tubes to a fixed volume of enzyme solution at 37°C.

Observation was made at regular intervals and the time noted at which each lead weight dropped.

The pH of the solutions was taken immediately after each test and found to be practically unaltered.

(a) Pepsin 10 per cent

pH	1·0	1·6	2·6	3·4
Average period required for digestion	17·2	15·2	17·6	15·2 hours

(b) Pepsin 2 per cent

pH	1·0	1·6	2·6
Average period required for digestion	25·6	26·4	24·5 hours

CONCLUSIONS. There is little to choose between 10 per cent pepsin at pH 1·0, 1·6 and 2·6. The least acid solution, pH 3·4 showed definite signs of bacterial activity which may have accounted for the slightly higher rate of digestion in this case.

The digestion period with 2 per cent pepsin was considerably longer and indicated that a minimal enzyme concentration was being approached.

A /

A solution containing 10 per cent pepsin "10000 test" at pH 1·6 appears to give optimum conditions.

EXPOSURE OF CATGUT TO ENZYME ACTION.

The way in which the enzyme is allowed to act upon the catgut under test is of primary importance - a factor which some workers appear to have overlooked. In particular, it is most undesirable that the strands should be free to untwist for this, as mentioned in connection with animal implant experiments, p. 18, multiplies greatly the surfaces at which digestion can take place. It could not be assumed that all types of catgut would untwist at the same rate and to the same extent.

Methods have been described[5, 17,] in which one end of a catgut strand was fixed in the enzyme solution and the other led out of the incubator to a weight and an electric clock contact. A disadvantage of this method is apparent in a description of apparatus for testing twelve strands at a time and involving the use of twelve electric clocks.

Jenkins and others[17] favoured a method whereby 2 gramme lead weights were supported by individual catgut strands in separate tubes. It is significant that the digestion periods obtained by this method were approxi-

mately /

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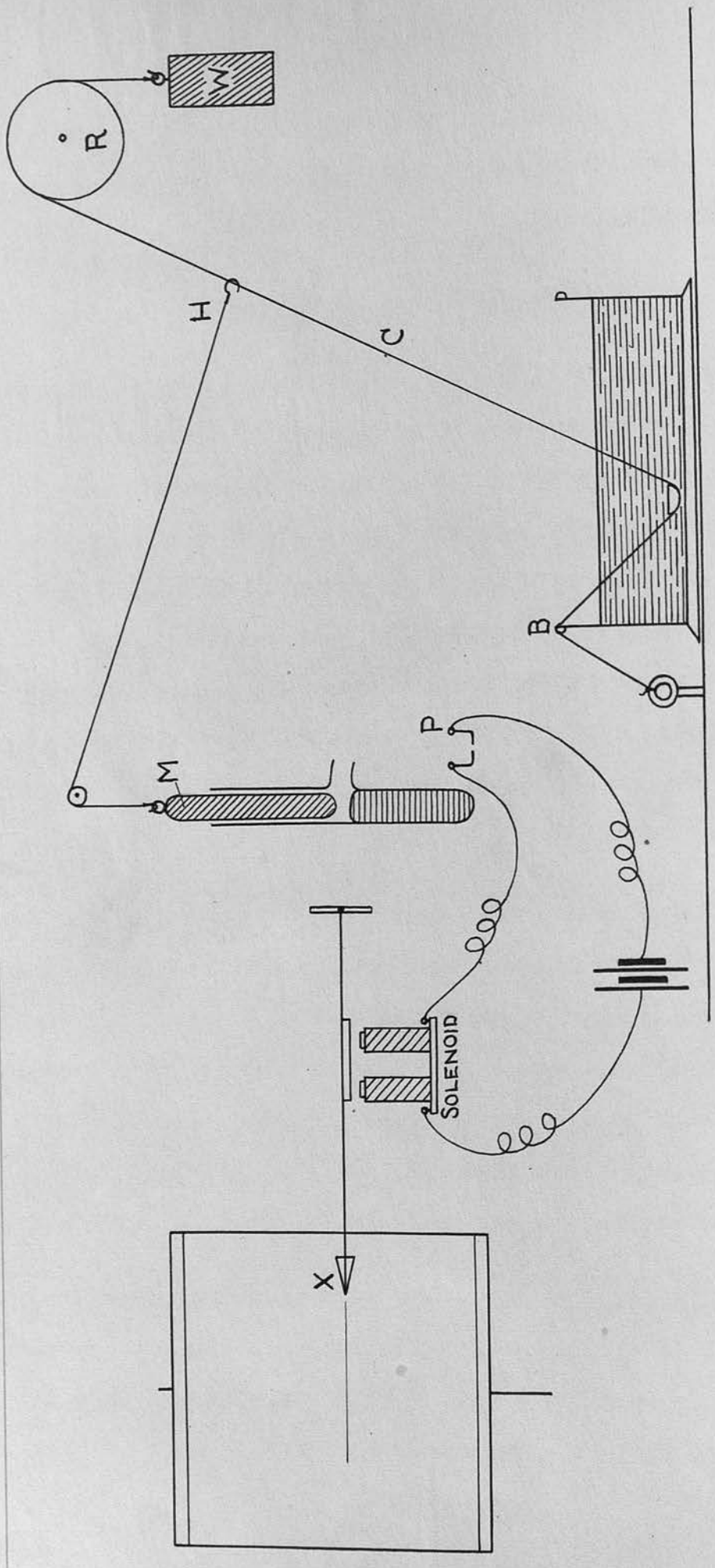

FIGURE 1.

mately 2½ times faster than those in which a 30 gramme weight was used.

An apparatus is desirable in which some approximation can be made to the physical strains to which catgut might be subjected in a wound.

It can be assumed that a severe wound test for catgut would be one in which about six interrupted stitches were required to hold in apposition the edges of a muscle incision with a force of 450 grammes. Also, that healing was slow in taking place, i.e. in relieving the strain on the stitches, so that if one or more stitches digested prematurely the additional strain would be thrown on to the remaining sutures. There must, of course, be no opportunity for the catgut to become untwisted.

To comply with these requirements a catgut digestion apparatus was devised.

THE "PROPORTIONATE LOAD" CATGUT DIGESTION APPARATUS.

The theoretical diagram, Fig.1, shows the principle of the present apparatus. A weight, W, is attached to a sample catgut string, C, which passes over a roller, R, through a glass dish containing pepsin solution (in which it is held immersed by a fixed perforated glass strip) /

strip) and out to a fixed ring to which it is tied.

When the portion of the catgut within the pepsin has been digested to such extent that it can no longer withstand the pull of the weight, it breaks and thus sets free a hook, H, attached by fine silk to a weight of 10/10½ grammes, M. The weight M falls into a well containing mercury, some of which is displaced and, closing momentarily an electric circuit as it passes the contacts, P, causes a break to the otherwise continuous line being recorded by the stylo, X, on a revolving drum.

In practice, there are six strands of catgut and six weights, W, each with its own mercury "switch".

Essential measurements are:-

Length of catgut strand from B to R = 12·5 in.
" " " in pepsin solution = 2·0 ".
Volume of pepsin solution = 50 ml.

The actual apparatus used is shown in the accompanying photographs, the incubator being omitted for clarity, Figs. 2 and 3; it is set up and functions as follows:-

Six strands of catgut are taken from the tubes, opened out and allowed to dry for a few minutes at a temperature between 16°C and 21°C in a relative humidity between /

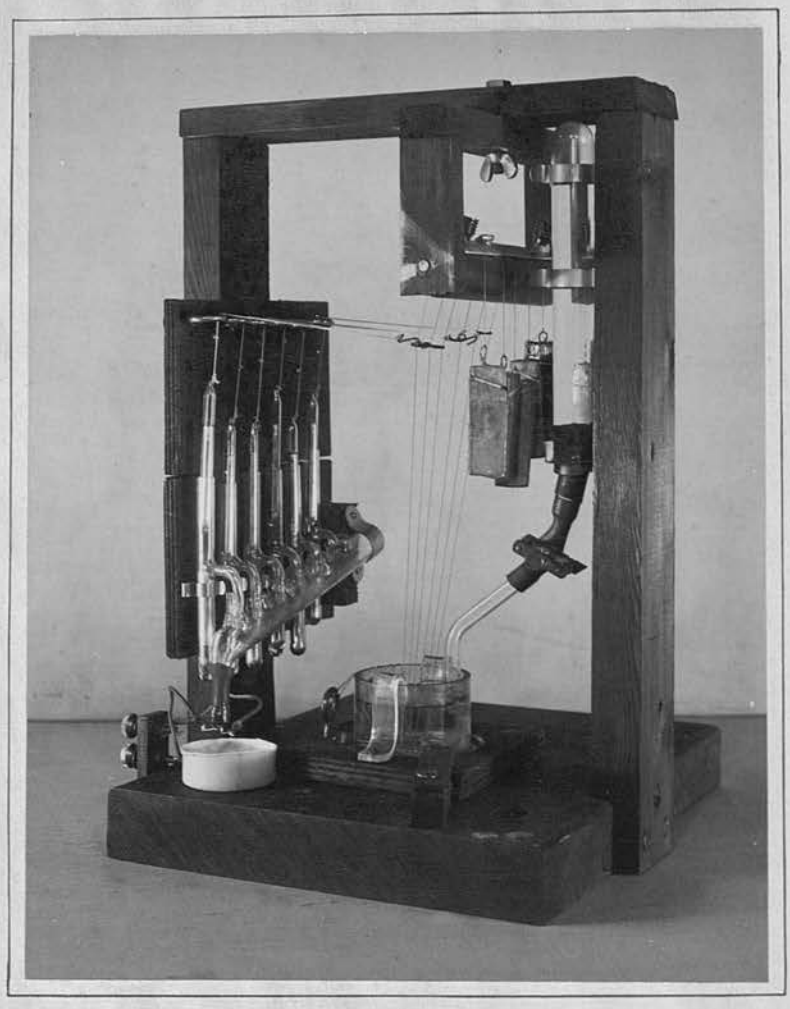

FIGURE 2. 1/3 ACTUAL SIZE.

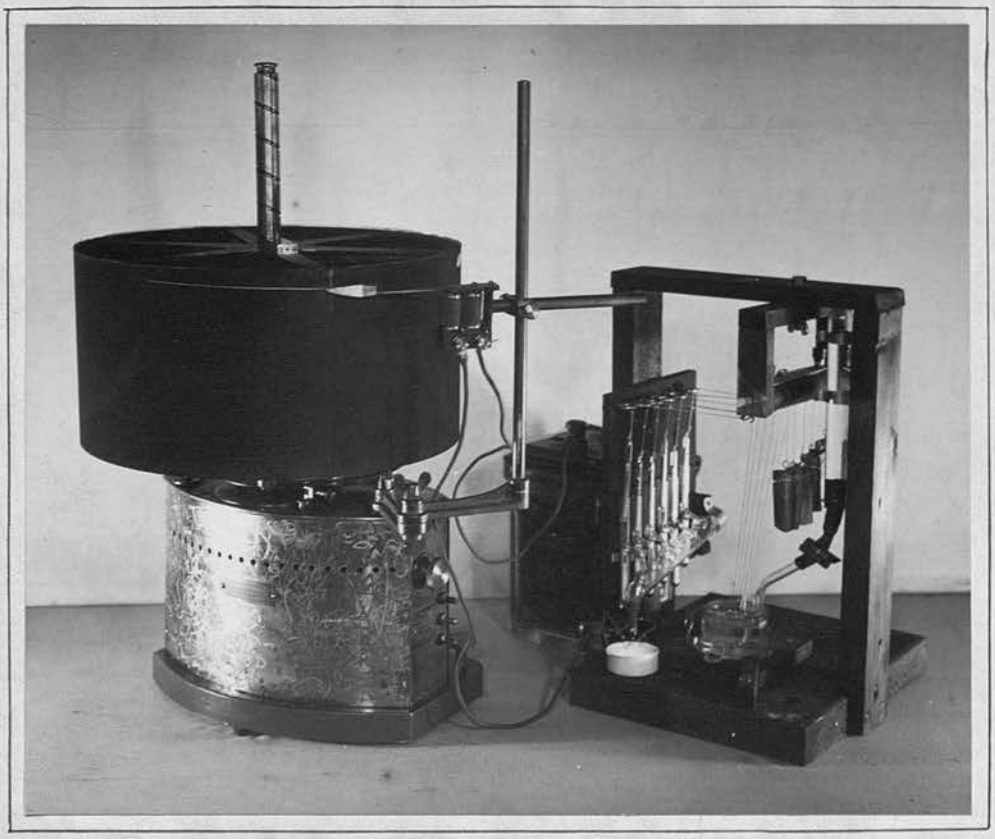

FIGURE 3. 1/5 ACTUAL SIZE.

between 60 per cent and 80 per cent. The strands are then tied to a ring on the base of the apparatus, passed through individual holes in a strip of glass or perspex fixed $\frac{1}{8}$ in. above the bottom of the pepsin dish and up over the roller. To the free end of each is fastened a 75 gramme weight so that there is then an equal strain on each strand. A long convex metal strip on top of the roller is then screwed down on to the six strands so that a total weight of 450 grammes is distributed equally over them.

A solution containing 10 per cent "10000 test" pepsin in dilute hydrochloric acid to pH 1·6 is then poured into the dish and a reservoir of distilled water is set up with an outlet tube just reaching the surface of the pepsin solution to replace loss by evaporation.

To each catgut strand there is then hooked a weight suspended above a mercury well (making a total strain over the six strands somewhat over 500 grammes); the apparatus is then placed inside an incubator to maintain a temperature of 37°C <u>in the pepsin solution</u> and electric leads are taken from the platinum contacts to a battery and solenoid acting on the stylo of a revolving drum outside the incubator.

As each catgut strand breaks through digestion a vertical mark is made on the otherwise straight line traced /

traced by the stylo on the drum. With the drum speed known, the time at which each catgut strand breaks can be calculated.

There is the possibility that several strands may break simultaneously with only one mark on the drum but in actual practice this occurrence is so rare as to be of no importance. Even when strands break within a few seconds of each other there is usually clear evidence of this on the drum.

It will be noted that, when one strand has broken the whole original strain is then redistributed over the remaining strands and the last strand to break does so under the total load of over 450 grammes.

EXPERIMENT D - 2. Before placing reliance on actual pepsin digestion tests a control experiment was performed using Standard Plain No. 2/0 catgut.

The apparatus was set up as described but pure distilled water was used in the dish instead of pepsin solution. There was practically no weakening of the catgut after four days.

The experiment was then repeated using a solution of hydrochloric acid at pH 1·6, without pepsin. Again there was no marked weakening of the catgut after four days.

EXPERIMENTS /

EXPERIMENTS. A large number of tests has been made by the above method on five of the catgut samples made under controlled conditions and on four commercial samples specially chosen for comparison.

The experimental results within each type showed consistency comparable with that obtained in the living tissue absorption tests. The relative rates of digestion of the different types were not always comparable with the absorption rates found in living tissue tests.

TABLE 8.

RESULTS OF PEPSIN DIGESTION TESTS ON VARIOUS SAMPLES OF CATGUT USING THE "PROPORTIONATE LOAD" APPARATUS.

1. Standard Plain No.2/0	Average digestion period		22·5	hours
2. Heat-sterilised ($1·0\%Cr_2O_3$) No. 2/0	"	"	52	"
3. Heat-sterilised ($0·1\%Cr_2O_3$) No. 2/0	"	"	27	"
4. Iodine-sterilised plain (i) No. 2/0	"	"	19	"
5. Iodine-sterilised plain (ii) No. 2/0	"	"	70·5	"
6. Brand D plain	"	"	19.5	"
7. Brand D hardened	"	"	10	"
8. Brand E plain	"	"	7	"
9. Brand E hardened	"	"	35	"

In /

In Table 8 the in vitro digestion times have been averaged and show a logical sequence when compared with animal implants so far as samples 1, 2, 3 and 5 are concerned. Brand D, however, both plain and hardened, which had the greatest resistance to absorption of all the animal implant tests has an even shorter in vitro digestion period than Standard Plain catgut and, in this, it resembles sample 4, iodine-sterilised plain (i).

In Brand E, the plain variety has a very short pepsin digestion time but the hardened sample takes a position midway between the controlled chromic samples (Nos. 2 and 3, Table 8).

There is no doubt that these in vitro test discrepancies are due to the unavoidable use of an acid enzyme in conjunction with effects upon the action of the pepsin caused by peculiarities in the chemical constituents of the catgut samples.

Although previous workers have suggested pepsin digestion tests for controlling the absorbability of surgical catgut in living tissue the foregoing results show that they may not give a reliable comparison. Any use which is made of in vitro tests should be checked by animal implants.

CHEMICAL CONSTITUTION OF SURGICAL CATGUT.

A full investigation has been made into the chemical constituents of various types of catgut, using the procedures later outlined.

It was known that certain chemicals, notably chromium, were used to delay absorption of catgut in the tissues; that others, such as iodine, may be residual from sterilisation processes and that mercury may be used partly to assist in sterilisation and partly to maintain an aseptic area around the tissues in which the catgut is implanted.

It was thought that the presence of some of these chemicals might have a greater bearing upon absorption rate than had been realised and this now appears to be true.

EXPERIMENT - CHEMICAL ANALYSES AND GELLING TEST: OUTLINE OF ROUTINE FOLLOWED. All quantitative figures obtained for the chemical content of samples of catgut refer to the sample air-dried to constant weight at a temperature between 16°C and 21°C with a relative humidity between 60 per cent and 80 per cent. This was chosen in preference to, say, drying at 100°C because it is the condition in which the surgeon is most likely to receive the sample for use and agrees also with the procedure /

procedure laid down for physical tests in the catgut monograph of the British Pharmaceutical Codex 1934, Sixth Supplement (1944).

1. Each sample, after drying as above, cut into small convenient lengths and about 10 grammes, accurately weighed, ashed to constant weight. Weight of ash taken.

2. Ash extracted with boiling distilled water for thirty minutes; filtered; residue washed.

Filtrate evaporated to dryness to constant weight at 100°C; weighed (water-soluble ash).

Residue dried to constant weight at 100°C; weighed (water-insoluble ash).

3. Water-soluble ash. Dissolved in distilled water and tested for metals by -

(i) Addition of dilute HCl.....Pb, Ag, Hg*

(No Pb or Ag in any sample).

(ii) Solution saturated with H_2S...Bi, Cu, Cd, As, Sb, Sn, Hg*

(No Bi, Cu, Cd, As, Sb or Sn in any sample).

*Hg was sought separately because it was normally lost by volatilisation during the preliminary ashing.

(iii) H_2S boiled off; added NH_4Cl (solid) and NH_4OH; acidified with acetic acid; added sodium acetate.

(This /

(This procedure was followed as a routine because exploratory tests had shown phosphate to be a normal constituent of catgut). Boiled (to ppt Fe when present). Added $FeCl_3$ to slight excess to complete precipitation of phosphate and boiled to remove excess Fe. Filtered[a].

Residue[a]. Dissolved in warm HNO_3, added $(NH_4)_6Mo_7O_{24}$ to ppt phosphate which was filtered off, dried to constant weight in dessiccator and weighed as $(NH_4)_3PO_4 \cdot 12MoO_3$.

Filtrate[a]. Added NH_4OH ..... Al, Cr. Filtered[b].

(No Al in any sample).

Chromium ppt.[b] dissolved in boiling water with aid of Na_2O_2, acidified with dilute H_2SO_4 and estimated chromium volumetrically with KI and $Na_2S_2O_3$.

(iv) Filtrate[b] saturated with H_2S ... Co, Ni, Mn, Zn.

(No Co, Ni, Mn or Zn in any sample).

(v) Boiled to remove H_2S, added solid $(NH_4)_2CO_3$. Boiled and filtered[c] ... Ca, Ba, Sr.

(No Ba, or Sr in any sample).

Residue[c] dissolved in hot dilute CH_3COOH, added $(COONH_4)_2$ and washed by centrifuging. Decomposed the $(COO)_2Ca$ with dilute H_2SO_4 at 60°C and estimated Ca indirectly with N/100 $KMnO_4$.

(vi) Filtrate[c]. Added solution of Na_2HPO_4 ... Mg. Filtered[d].

Residue[d] ignited and weighed as $Mg_2P_2O_7$.

Filtrate /

Filtrate[d]. Any K present ignored.

4. Water-insoluble ash. Extracted with boiling dilute HCl[e] for 30 minutes ... Pb, Ag, Hg and some Cr and Fe.

(No Pb or Ag in any sample. Hg estimated separately as previously stated).

(vii) Acid-insoluble ash[e] ignited, fused with Na_2O_2, extracted with water from any residual Fe_3O_4 and chromium assayed as before.

(viii) HCl solution[e] examined as described under water-soluble ash.

5. Total and combined iodine. About 5 grammes of air-dried sample, accurately weighed, digested in 200 mils of distilled water at 37°C overnight. Repeated until all soluble halide was extracted.

(ix) Residual gut, free from soluble halide, dried at 100°C. Added 25 mils N/10 $AgNO_3$ in conc. HNO_3 and left until organic matter was destroyed. Titrated with NH_4CNS to obtain combined iodine content.

(x) To obtain the total iodine figure a fresh sample of gut was taken and treated with N/10 $AgNO_3$ in conc. HNO_3 as described above, omitting the preliminary digestion with water.

(xi) The procedures described under (ix) and (x), above, actually gave "Halide" (Cl, Br and I). Where the figure obtained exceeded 0·06 per cent the following

(xii) /

(xii) routine was adopted in order to confirm that the excess was due to iodine.

(xii) Recovered the residue (silver halide and silver thiocyanate) from the back titration of excess $AgNO_3$ with NH_4CNS and fused in a platinum crucible with Na_2CO_3 and K_2CO_3. Dissolved and transferred to a stoppered bottle, added an equal volume of HCl and titrated with M/20 KIO_3, using $CHCl_3$ as indicator.

6. Mercury. About 5 grammes of air-dried sample, accurately weighed, were transferred to a Kjeldhal flask and dissolved by "wet oxidation" with conc. H_2SO_4 and conc. HNO_3. When all carbon had been removed the solution was boiled down to remove oxides of nitrogen. Transferred to a beaker, made alkaline with NH_4OH, then just acid with HCl and saturated with H_2S. Filtered off any ppt through a tared sintered glass crucible, washed with solution of H_2S, dried at 100°C, weighed HgS and returned as Hg.

Confirmation of the above was obtained as follows (xiii) and (xiv).

(xiii) Hg present in macro proportion. Dissolved the weighed HgS in aqua regia, added a little conc. H_2SO_4 and boiled until chlorine and oxides of nitrogen had been removed. Neutralised, added excess KI, NaOH solution and 40 per cent HCHO solution; allowed to stand for 30 minutes at about 25°C. Added excess CH_3COOH /

CH_3COOH and excess standard iodine solution; allowed to stand until pptd mercury was all dissolved. Titrated residual iodine with $Na_2S_2O_3$ to obtain figure for Hg.

(xiv) Hg present in micro proportions. Dissolved the suspected HgS ppt in aqua regia, diluted slightly with water, added a small piece of bright copper foil and left for 30 minutes. Removed the Cu foil to a small test-tube, drew out the open end to form a narrow neck, placed a small crystal of iodine well away from the foil and plugged the open end of the tube. On heating the end of the tube containing the foil strongly, formation of red HgI_2 in the constricted portion of the tube confirmed the presence of Hg.

7. Mercury in tubing fluid. Evaporated a convenient measured volume of the tubing fluid on a water bath to remove the alcohol, transferred the residue to a Kjeldhal flask and proceeded as under (6) above.

Gelling test. Two grammes of air-dried sample (cut into short lengths, 2 - 3 mm) were refluxed with 100 mils of distilled water for one hour, taking care to keep the pieces submerged.

Filtered and concentrated to 15 mils and allowed to stand overnight in a flat-bottomed porcelain dish, free from dust.

Examined /

Examined empirically and reported as follows:-

Very firm gel	++
Definite gel	+
Borderline case	±
Mobile fluid	-

It was found by experiment that larger quantities of soluble chromium salts than were likely to be met with in practice had no effect upon gel formation.

Some samples containing mercury tended to give an atypical result.

An experiment was performed to determine the possible effect upon gel formation of variation in the degree of comminution of the sample. It was found that no great difference in result obtained until the variation in length of the pieces of gut was five times the average 2 - 3 mm length used.

TABLE 9 /

TABLE 9.

ANALYSES OF VARIOUS TYPES OF CATGUT.

SAMPLE	TOTAL ASH	CALCIUM (As Ca)	CHROMIUM (As Cr_2O_3)	IODINE		MERCURY (As Hg)		GELLING TEST
				TOTAL	COMBINED	IN GUT	IN FLUID	
Brand A plain No. 2/0	0·68	0·31	Nil	0·13	trace	Nil	Nil	±
Brand A hardened No. 2/0	0·82	0·25	0·40 (50% sol)	0·43	0·13	Nil	Nil	-
Brand B plain No. 2/0	0·34	0·06	Nil	1·07	1·07	Nil	Nil	+
Brand B hardened (i) No. 2/0	0·31	0·04	Nil	1·09	1·09	Nil	Nil	±
Brand B hardened (ii) No.2/0	0·21	0·02	trace	1·40	1·40	Nil	Nil	++
Brand C plain No. 2/0	1·76	0·44	0·22	1·80	1·25	trace	0·006	-
Brand C hardened No. 2/0	1·90	0·64	0·72 (75% sol)	1·91	1·12	trace	<0·002	-
Brand D plain No. 2/0	0.77	0·18	Nil	0·95	0·95	0·10	0·004	±
Brand D hardened No. 2/0	1·11	0·10	0·18 (95% sol)	1·55	1·55	0·47	0·004	±
Brand /								

TABLE 9 (Continued).

SAMPLE	TOTAL ASH	CALCIUM (As Ca)	CHROMIUM (As Cr_2O_3)	IODINE TOTAL	IODINE COMBINED	MERCURY (As Hg) IN GUT	MERCURY (As Hg) IN FLUID	GELLING TEST
Brand E plain No. 2/0	0·75	0·30	Nil	2·11	1·24	trace	0·01	±
Brand E hardened No. 2/0	1·38	0·29	0·59 (36% sol)	1·88	1·49	trace	0·01	±
Standard Plain No. 2/0	0·64	0·06	Nil	0·05	0·05	Nil	Nil	+
Standard Plain with HgI_2 No. 2/0	-	-	Nil	1·26	1·26	0·26	0·004	-
Standard Plain No. 2	0·64	0·06	Nil	0·05	0·05	Nil	Nil	+
Heat-sterilised (0·1% Cr_2O_3) No. 2/0	0·45	0·16	0·10	0·06	0·06	Nil	Nil	+
Heat-sterilised (1·0% Cr_2O_3) No. 2/0	1·20	0·07	1·05	0·06	0·06	Nil	Nil	-
Heat-sterilised (1·0% Cr_2O_3) No. 2	1·20	0·07	1·00	0·06	0·06	Nil	Nil	-
Iodine-sterilised plain (i) No. 2/0	1·02	0·04	Nil	0·69	0·69	Nil	Nil	-

Iodine /

TABLE 9 (Continued).

SAMPLE	TOTAL ASH	CALCIUM (As Ca)	CHROMIUM (As Cr_2O_3)	IODINE		MERCURY (As Hg)		GELLING TEST
				TOTAL	COMBINED	IN GUT	IN FLUID	
Iodine-sterilised plain (ii) No. 2/0	0·72	0·06	Nil	1·15	1·15	Nil	Nil	-
Iodine-sterilised hardened No. 2/0	0·70	0·03	0·05 (100% sol)	1·15	1·08	Nil	Nil	-

All figures are expressed as percentages $^{w}/_{w}$ on air-dried catgut sample, except Hg in tubing fluid which is in percentage $^{w}/_{v}$ of fluid.

ANALYTICAL RESULTS.

Table 9 shows the results of analyses for calcium, chromium, iodine and mercury and of a gelling test.

A high ash figure may indicate presence of these elements but is not otherwise important.

In some cases soluble iodides (never free iodine) could be removed from the gut by digestion in water; where there was a marked amount of soluble iodide present this was generally associated with the presence of mercury and could be explained by the use of iodide as a solvent carrier for introduction of the Hg.

Magnesium, iron and phosphate were also tested for and found to be present in most cases but only in traces and it was not considered necessary to report exact figures. Sulphate was present in very few cases and appeared to have no significance.

A gelling test was devised (see p. 65) to find a possible relationship between ease of hydrolysis and resistance to absorption in the tissues.

Calcium content was variable and was probably due mainly to the water used in preparation of the raw catgut strings.

Chromium, when present, was not always in the same chemical /

chemical state. This was indicated in some cases by the colour of the catgut which varied from greenish/brown (basic state) to a scarcely detectable yellow (acidic state).

Chromium, especially when combined in the basic state with catgut protein, can delay absorption. This is seen in the difference between Standard Plain catgut (absorption Group I) and an otherwise comparable heat-sterilised (basic) chromic catgut containing 1 per cent Cr_2O_3 (absorption Group II).

In some samples, uncombined water-soluble chromium was present and it is noteworthy that these caused some of the few cases of detritus noted in the animal experiments and included two types of "hardened" catgut which came unexpectedly into absorption Group I.

Some importance is attached to the fact that a basic-chromed size 2/0 catgut made under controlled conditions and containing 1 per cent Cr_2O_3 (none free or water-soluble) caused no detritic reaction over many animal tests; even thick gut of the same type (size 2) caused only a very slight reaction whereas Standard Plain catgut <u>in size 2</u> caused a marked reaction.

A basic chromium content of 1 per cent Cr_2O_3 did not alone give full protection to the absorption period in /

in presence of wound contamination (see Table 6) - a point worth noting because it confirms the observation that chromium in combination with catgut does not have a harmful effect upon cell metabolism.

Iodine, when used for the sterilisation of surgical catgut definitely lengthens the absorption period. Iodine-sterilised catgut, prepared under carefully controlled conditions, did not cause detrimental tissue reaction and was as satisfactory as the best samples of heat-sterilised chromic gut. Some samples of an iodine-sterilised commercial brand which had an acid reaction caused detritus in rabbit muscle.

Catgut which, on chemical analysis, gives a high "combined iodine" figure has not necessarily been iodine-sterilised. It will be seen that Standard Plain catgut with HgI_2, which was sterilised by heat, gave a combined iodine figure of 1·26 per cent due to iodide used as a solvent carrier to introduce the mercury.

It should be noted that catgut which has not been treated with iodine or iodide gives a "combined iodine" value up to 0·06 per cent which is due to naturally occurring halide.

Mercury in catgut delayed absorption, probably as a result of its known function as a protein inactivator. It will be noted from Table 11 that the presence of 0·26 per /

per cent Hg was sufficient to retain Standard Plain catgut in absorption Group II.

The presence of a small amount of mercury in catgut probably has no harmful effect though the use of larger quantities as an inhibitory agent to replace true sterilisation is not to be recommended.

TABLE /

TABLE 10.

CO-RELATION OF ABSORPTION-PERIOD GROUPS WITH CHEMICAL ANALYSES AND GELLING TESTS.

ABSORPTION GROUP	CATGUT SAMPLE	TOTAL ASH	Ca	Hg in Gut	Cr_2O_3	"COMBINED IODINE"	GELLING TEST
I	Standard Plain No. 2/0	0·64	0·06	Nil	Nil	0·05	+
	Brand A plain No. 2/0	0·68	0·31	Nil	Nil	trace	±
	Brand A hardened No. 2/0	0·82	0·25	Nil	0·40	0·13	-
	Brand E hardened No. 2/0	1·38	0·29	trace	0·59	1·49	±
II	Standard Plain with HgI_2 No. 2/0	-	-	0·26	-	1·26	-
	Heat-sterilised (1·0%Cr_2O_3) No. 2/0	1·20	0·07	Nil	1·05	0·06	-
	Heat-sterilised (0·1%Cr_2O_3) No. 2/0	0·45	0·16	Nil	0·10	0·06	+
	Brand E plain No. 2/0	0·75	0·30	trace	Nil	1·24	±
	Brand B plain No. 2/0	0·34	0·06	Nil	Nil	1·07	+
	Brand B hardened (ii) No. 2/0	0·21	0·02	Nil	trace	1·40	++
	Brand C plain No. 2/0	1·76	0·44	trace	0·22	1·25	-
III /							

TABLE 10 (Continued).

ABSORP-TION GROUP	CATGUT SAMPLE	TOTAL ASH	Ca	Hg in Gut	Cr_2O_3	"COMBINED IODINE"	GELLING TEST
III	Brand B hardened (i) No. 2/0	0·31	0·04	Nil	Nil	1·09	±
	Iodine-sterilised plain (i) No. 2/0	1·02	0·04	Nil	Nil	0·69	-
	Iodine-sterilised plain (ii) No. 2/0	0·72	0·06	Nil	Nil	1·15	-
	Iodine-sterilised hardened No. 2/0	0·70	0·03	Nil	0·05	1·08	-
	Brand C hardened No. 2/0	1·90	0·64	trace	0·72	1·12	-
	Brand D plain No. 2/0	0·77	0·18	0·10	Nil	0·95	±
	Brand D hardened No. 2/0	1·11	0·10	0·47	0·18	1·55	±

In Table 10, chemical constituents are shown in relation to absorption Groups. If the catguts made under controlled conditions are studied the following relationships will be seen:-

TABLE 11.

CATGUT SAMPLE	PRESENT	ABSENT	GELLING TEST
GROUP I			
Standard Plain No. 2/0	-	Hg, I Cr_2O_3	+
GROUP II			
Standard Plain with HgI_2 No. 2/0	Hg comb. I	Cr_2O_3	-
Heat-sterilised (1·0% Cr_2O_3) No. 2/0	Cr_2O_3	Hg, I	-
Heat-sterilised (0·1% Cr_2O_3) No. 2/0	Cr_2O_3	Hg, I	+
GROUP III			
Iodine-sterilised plain (i) No. 2/0	I	Hg Cr_2O_3	-
Iodine-sterilised plain (ii) No. 2/0	I	Hg Cr_2O_3	-
Iodine-sterilised hardened No. 2/0	I Cr_2O_3	Hg	-

From this it will be seen that the presence of mercury or chromium may put catgut into absorption Group II and combined iodine due to sterilisation with iodine may put it into absorption Group III. A negative /

negative gelling test indicated Groups II or III with the exception of the heat-sterilised catgut containing only 0·1 per cent Cr_2O_3; in this case the chromium was introduced in the acidic state.

There are indications that iodine, chromium and mercury may combine with catgut in various ways and that the state of such combination in the protein molecule has a direct bearing upon absorption rate.

Some of the apparent anomalies amongst other samples of catgut in Table 10 are explained as follows:-

Brand A hardened No. 2/0, in Group I: 50 per cent of the chromium was water soluble.

Brand E hardened No. 2/0, in Group I: 35 per cent of the chromium was water-soluble. The high combined iodine figure is probably due to the use of biniodide of mercury. (This brand of catgut is said to be heat-sterilised).

Brand E plain No. 2/0, in Group II: Probably due to its mercury content; the animal absorption tests showed it to be not far outside Group I.

Brand /

Brand B plain No. 2/0 and Brand B hardened (ii) No.2/0:	Understandably in Group II through their iodine-sterilisation but gave +ve gelling tests which may be connected with the fact that these samples of gut had an acid reaction.
Brand C plain No. 2/0, in Group II:	Explained by presence of Cr_2O_3, Hg and I.
Brand B, hardened (i) No. 2/0, in Group III:	Is again explained by iodine used in sterilisation.

SUMMARY AND CONCLUSIONS.

1. The existence of different types of surgical catgut has been confirmed and their fundamental differences investigated.

2. The main types found in commerce have been reproduced under controlled conditions and compared with each other and with samples obtained in the open market.

3. The reasons for these differences - which are mainly reflected in absorption rates - have been sought and largely explained by comparing the chemical constitutions of the catguts with their behaviour in living tissues. /

tissues.

4. Reference has been made to results obtained by previous workers and the lack of a basis for comparisons of absorbability remedied by the production of a Standard Plain catgut.

5. A technique has been devised whereby a practicable comparison can be made in living tissue between the absorption rates of different types of catgut and in which the sutures to be tested are observed in circumstances strictly analogous to those obtaining at actual operation.

6. From 5 (above) it appears that no attempt should be made to produce catgut in more than two or three absorption groups.

7. The over-riding effect of sterilisation methods on absorption rates has been shown. Although the durations intimated on labels are frequently at variance with the actual resistance of the catgut to absorption, the error has mainly been found to be on the "safe" side; that is, the period for which the sutures retain effective holding power is generally in excess of that claimed.

8. Excessive reaction of the tissues to catgut, which has been put forward by various workers as a reason for using /

using non-absorbable suture materials, has been shown to be avoidable by using fine gauges - a procedure which is justified not merely by the absence of undesirable effects but also by the fact that fine catgut has ample tensile strength. Advocates of the use of non-absorbable suture materials to the partial or complete exclusion of catgut have not been lacking[8,21], but experiment demonstrated that several non-absorbable materials were themselves not without a reactive effect. Moreover, although some non-absorbable materials may be more desirable than others, the fact remains that catgut is ultimately absorbed and no unaltered foreign bodies remain which might become a focus for trouble at some future time.

9. From this present investigation and confirming the observations of other workers, it is recommended that genuinely plain catgut should never be used except in the very finest gauges; and, even then, only for surface suturing.

10. As a result of the co-relation of the chemical constituents of catgut with its absorption rate in the tissues, it is suggested that this could be used as an adjunct in controlling and determining the absorption group into which the finished product is required to fall.

11. The "proportionate load" apparatus has been devised as being the most satisfactory means for performing /

forming in vitro digestion tests but the results obtained indicate that reliance should not be placed on this method alone for determining the absorption rate of catgut in the tissues. It is quite possible, however, that it would serve as a routine laboratory control in that fluctuations in the absorbability of the finished product might be revealed, but the main reliance should be placed on implants in living tissue.

12. Finally, the suggestion is offered that a living tissue test, based on the technique already described, might be considered by the authorities concerned for addition to the existing standards for surgical catgut using Standard Plain catgut as a reference and prescribing not more than three absorption period Groups.

This work has been mainly carried out in the Wilkie Surgical Research Laboratory, University of Edinburgh, by kind permission of Professor J. R. Learmonth.

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